

October 8, 2004

TO: Ms. Jeanine Goldberg FAX: 571-273-0743
U.S. Patent & Trademark Office

FROM: Khue Nguyen, Ph.D.
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RE: Patent Application # 09/938,013

Please find attached a copy of my October 7, 2004 letter to you.

October 7, 2004

Ms. Jeanine Goldberg
Art unit 1634
US Patent & Trademark Office
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Ms. Goldberg:

The following is in regards to Patent Application # 09/938,013, entitled "Utilization of nucleotide probes for the measurement of specific mRNA for the molecular diagnosis of autosomal recessive spinal muscular atrophy."

Realizing that the examiner holds the power to accept or reject the patent application, based on his/her interpretation of the regulations and the application of such regulations to the specific case, the applicant nevertheless feels that this process should be made clear.

The examiner's 6/4/04 communication of final rejection of the application reflects inconsistencies and inaccuracies that need clarification. For this reason, the applicant requested the 9/9/04 phone conference to seek the examiner's clarification and explanation relating to the specific focus of the application; to facilitate such a process, the applicant faxed ahead of time a draft of the key points (Fax 9/7/04), with the hope that they would be adequately addressed. Unfortunately, however, the applicant repeatedly received insistence that he retains an attorney and that the examiner and Dr. Benzion (the examiner's supervisor) would only talk to an attorney. The point is: The applicant requested the examiner to merely clarify what she wrote; it hardly requires the services of an attorney to receive these clarifications.

During the 9/9/04 phone conference, certain points were reiterated by the examiner – that the applicant's work is novel, that claim language once modified as suggested would overcome the rejection, and that the main issue at hand is the matter of obviousness and non-obviousness. Most of the questions and issues raised by the applicant were not adequately answered or clarified.

Point c) in Fax 9/7/04 was not addressed: "It is not clear as to why sometimes you stated that Jong's method is semi-quantitative (pages 11, 14, 16 of 6/4/2004 Office communication) and sometimes you stated that Jong's method is quantitative by stating that "the ratio is a quantitative method" (page 11 of 6/4/2004 Office communication), and by saying that "Jong teaches performing quantitative analysis by determining the ratio of exon 7..." (page 15 of 6/4/2004 Office communication) which is a misunderstanding on your part because the ratio has nothing to do with characterizing the type of method used in order to get the results of the experiments; the research method used can be qualitative, semi-quantitative or quantitative..."

-Refusal to address the question on the part of Dr. Benzion and the examiner and their insistence on talking only to an attorney had pushed the applicant to raise the question as to whether the examiner has the adequate background to evaluate this type of application.

Point b) in Fax 9/7/04 was not adequately addressed: "... I do not understand why, in the 6/4/04 communication, you however talked about the various techniques used for various purposes but not specifically applied for SMA diagnostic purpose"

-Dr. Benzion said that the applicant has to prove that the quantitative method for SMA diagnosis is what people are looking for.

-This matter has already been shown in the literature.

Point a) in Fax 9/7/04 was not adequately addressed: "I do not understand why you still maintain the issue of new matter in the last Office communication (6/4/2004) while you had already accepted my clarification that there is no new matter as per my phone discussion with you on 1/20/2004 and following my 12/9/2003 FAX. On July 15, 2003 you said that you would not pursue the examination of the application unless the issue of new matter is resolved; the fact of the matter is that you have accepted that there is no new matter by the very fact that you have continued to examine my application."

-Dr. Benzion replied that "the examiner had to write a response"

-Ms. Goldberg acknowledged the applicant's work is novel but said it is "obvious."

On the issue of obviousness and non-obviousness, Dr. Benzion gave numerous examples that did not relate to the specific focus on hand, except that he said if others had previously taught a semi-quantitative method for SMA diagnosis, one would then be motivated to come up with a quantitative method. This statement actually warrants a serious look at how the clause obviousness/non-obviousness is interpreted and applied.

When one makes such a statement (as mentioned above), one could also say: In order to deal with infection of HIV responsible for AIDS, one would be motivated to prevent the production of HIV, 1) by blocking the uptake of HIV into the human cell, or 2) by blocking viral DNA replication in human cells. Yes, this is well known and easy to say; the fact of the matter, however, is that no one so far has been able to find a way to do this.

Related to the specific case of this application, the current practice has been the use of a qualitative method of SMA diagnosis which has shown not to be adequate, there has thus been an obvious motivation to seek a quantitative method. So far, however, others were only able to come up with a semi quantitative method. No one before this application was able to develop a quantitative method for the molecular diagnosis of SMA. There is thus a distinction between knowing what is obviously needed, knowing what should be done next and actually developing or inventing what is needed.

Furthermore, applying the U.S.C. 103 (a) clause on obviousness/non-obviousness based on misunderstanding of information or inaccurate knowledge is a serious concern.

In the 6/4/04 communication, the examiner seems to try to demonstrate that others' previous work used a "quantitative" method because they used ratio in the data analysis – this is incorrect. As explained in the 9/7/04 fax, using the ratio is for the purpose of correcting the fluctuations of the PCR reaction in order to accurately compare the results from one sample to another; using ratio has nothing to do with what type of method is being used: Qualitative, semi quantitative or quantitative. Statements such as "more quantitative method" (page 16, 6/4/04 communication) is also a concern; a method is either qualitative, semi quantitative or quantitative. There is confusion and inconsistency in the examiner's comments about previous work using quantitative and semi quantitative method for SMA diagnosis despite the fact that the authors of such previous work (Jong et al.) themselves clearly specified the use of a semi quantitative method for SMA diagnosis.

The fact of the matter is that, prior to this application, there is no quantitative method for the molecular diagnosis of SMA. The fact of the matter is that, in this application, the approach that permits the quantification, i.e., the identification of the numbers of transcripts (mRNA) specific to SMN (survival motor neuron, the gene associated with SMA) for SMA diagnosis is totally different from the approach used in previous work on semi quantitative method for SMA diagnosis (see comparison in Fax 5/24/04).

The examiner's comments about various known techniques such as probes and mRNA are not relevant to this application, nor consistent with the cited law; these techniques were used for other purposes and none was used for SMA diagnosis prior to this application. The fact of the matter is that no one prior to this application has thought of, nor successfully combined the various techniques in order to develop the quantitative method for molecular diagnosis of SMA at the mRNA level. The fact of the matter is that no one before this application has used probes to detect SMA at the mRNA level.

The examiner's rejection based on how the invention was made in the 6/4/04 communication does not seem to reflect the section of the cited law, "Patentability shall not be negated by the manner in which the invention was made."

The examiner's statement, "The instant application appears to take a well known disease and a well known mutation and detect and quantify using well known detection and quantification means. This combination of prior methods does not constitute an unobvious contribution over the art" 1) appears to be inconsistent with the cited law, "Patentability shall not be negated by the manner in which the invention was made;" 2) appears to indicate that, according to the examiner, all previous U.S. patented inventions had been incorrectly assessed because there is no invention that does not use prior known means or devices previously applied for other purposes to create a new invention. For example, this applicant had previously received the U.S. patent for a method of dissolving preformed beta-amyloid peptide fibrils in vitro by poly-L-lysine (U.S. Patent No. 6,639,058). Poly-L-lysine is a well known compound used for a variety of other purposes that was used to dissolve preformed beta-amyloid peptide fibrils found in the brains of people with Alzheimer's disease, a well known disease. In other

words, according to the examiner, it appears that, if a gear, a wheel, or a coil (previously well known device and function) is used in an invention, then it would not be patentable.

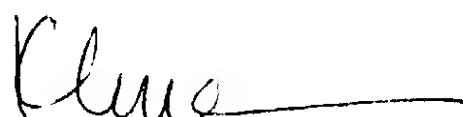
In brief, it has not been demonstrated clearly as to what the examiner's interpretation of the cited U.S.C. 103 (a) clause is and how such interpretation is applied to the specific case of this application.

It has not been demonstrated clearly as to how U.S.C. 103 (a) is interpreted and applied in the rejection of this application, while the examiner has acknowledged that the development of a quantitative method would be an improvement of Jong's semi-quantitative method (page 16 of the 6/4/2004 Office communication). By this very statement the examiner thus acknowledges patentability under the cited law.

Finally, the applicant does not believe that lawmakers had the intention to make the patenting application process to be prohibitive for inventors who cannot afford to incur the high cost of an attorney.

The applicant recognizes that the field of this application is a difficult area of molecular biology which required a lot of hard work for the examiner; and this is appreciated. The applicant recognizes and accepts the suggestion of the examiner to modify the claiming and other language and wording issues. However, final rejection of this application based on inconsistencies and unclear grounds is a serious concern and should not have been made. The applicant thus hopes that this situation would be rightfully rectified. Thank you.

Sincerely,

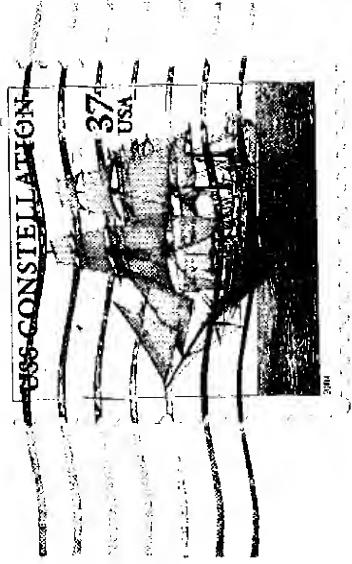
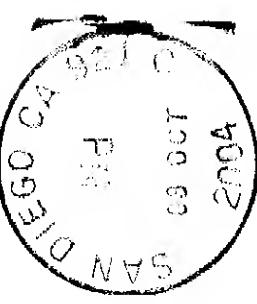


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